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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/031,874	11/14/2002	Jasmid Tanha	11054-1	8696

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EXAMINER	
BLANCHARD, DAVID J	
ART UNIT	**PAPER NUMBER**
1643	

DATE MAILED: 01/04/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/031,874	TANHA ET AL.	
	Examiner	Art Unit	
	David J. Blanchard	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 October 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-40* is/are pending in the application.

4a) Of the above claim(s) *10-24 and 31-40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/3/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-9 are cancelled.

Claim 25 has been amended.

Claims 10-24 and 31-40 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.

2. Claims 25-30 are under examination.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Information Disclosure Statement

4. The information disclosure statement (IDS) submitted on 10/3/2005 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the examiner has considered the IDS. Applicant is advised that certain documents cited on the IDS were previously cited and considered by the Examiner in a prior Office Action (see PTO-892 mailed 6/2/04). Additionally, the IDS filed 10/6/2005 is a duplicate of the IDS filed 10/3/2005.

Rejections Withdrawn

5. The rejection of claims 1-3, 5-9 and 25-30 under 35 U.S.C. 112, second paragraph as being indefinite for reciting "said fragments comprising fragments" is withdrawn in view of the amendments to the claims.

6. All of the rejections applied to claims 1-3 and 5-9 in the previous Office Action (mailed 5/3/05) are withdrawn in view of the cancellation of the claims.

Response to Arguments

7. The rejection of claims 25-29 under 35 U.S.C. 102(e) as being anticipated by Frenken et al [a] (U.S. Patent 6,399,763 B1, filed 1/19/2000) is maintained.

The response filed 10/3/05 provides a technical discussion of the differences between conventional variable heavy domains (VH) and VHH fragments. Applicant points out that VHH are structurally distinct from conventional VHs, which normally exist as part of the conventional four-chain immunoglobulin. Applicant submits that conventional heavy chain domains (VHs) are different from VHHs of camelids as described by Frenken et al [a]. This has been fully considered but is not found persuasive. First, the claimed camelid cDNA library recites that it comprises antigen-binding fragments of conventional variable heavy domains of camelid antibodies, which is inclusive to conventional VH and VHH in the library. Applicant is reminded that the transitional term "comprising" is inclusive or open-ended and does not exclude additional, unrecited elements or method steps (see MPEP 2111.03). Additionally, the dependent claims (e.g., claims 26-28 in particular) still recite that each antigen-binding fragment of the cDNA library comprises the "variable heavy domain (VHH or VH)" of the antibody, which clearly encompasses both conventional VHs and VHHs in the cDNA library. Further, Frenken et al [a] teach that the cDNA library of non-immunized lama (camelid) antigen-binding antibody fragments are obtained by the steps comprising (1)

isolating lymphocytes from a biological sample obtained form a non-immunized lama (see column 9, lines 63-66, in particular), (2) total RNA was isolated from the lymphocytes (see column 5, lines 66-67, in particular), (3) performing first-strand cDNA synthesis (i.e., reverse-transcribing) and DNA encoding antigen-binding fragments (i.e., cDNA) were amplified by PCR (see column 10, lines 4-5, in particular), (4) cloning the amplified antigen-binding fragments into a vector (see column 10, lines 51-52, in particular), and (5) recovering the obtained clones (see column 10, lines 62-65 and Examples 2-3, in particular), which is the identical process of present claim 25 for obtaining the conventional VH camelid domains from a non-immunized llama. Thus, it appears that Frenken et al [a] have produced a cDNA library that necessarily contains antigen-binding fragments that are identical to those recited in the present claims. Since the Patent and Trademark Office does not have the facilities for examining and comparing the claimed cDNA library with the cDNA library of Frenken et al [a], the burden of proof is upon the Applicants to show a distinction between the structural and functional characteristics of the claimed cDNA library and the cDNA library of the prior art, both produced from identical starting material (i.e., lymphocytes from a non-immunized llama) and produced by an identical process, i.e., isolating lymphocytes from a non-immunized llama, isolating total RNA from the lymphocytes, reverse transcribing the RNA and amplifying the cDNA sequences coding for the antigen-binding fragments (i.e., RT-PCR), cloning the amplified cDNA into a vector and recovering the obtained clones. See In re Best, 562 F.2d 1252, 195 U.S.P.Q. 430 (CCPA 197) and Ex parte Gray, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.).

8. The rejection of claims 25-29 under 35 U.S.C. 102(a) as being anticipated by Frenken et al [b] (WO 99/37681) is maintained.

The response filed 10/3/05 provides a technical discussion of the differences between conventional variable heavy domains (VH) and VHH fragments. Applicant points out that VHH are structurally distinct from conventional VHs, which normally exist as part of the conventional four-chain immunoglobulin. Applicant submits that conventional heavy chain domains (VHs) are different from VHHs of camelids as described by Frenken et al [b]. This has been fully considered but is not found persuasive. First, the claimed camelid cDNA library recites that it comprises antigen-binding fragments of conventional variable heavy domains of camelid antibodies, which is inclusive to conventional VH and VHH in the library. Applicant is reminded that the transitional term "comprising" is inclusive or open-ended and does not exclude additional, unrecited elements or method steps (see MPEP 2111.03). Additionally, the dependent claims (e.g., claims 26-28 in particular) still recite that each antigen-binding fragment of the cDNA library comprises the "variable heavy domain (VHH or VH)" of the antibody, which clearly encompasses both conventional VHs and VHHs in the cDNA library. Further, Frenken et al [b] teach that the cDNA library of a non-immunized lama (camelid) antigen-binding antibody fragments are obtained by the steps comprising (1) isolating lymphocytes from a biological sample obtained form a non-immunized lama (see page 13, lines 6-8, in particular), (2) total RNA was isolated from the lymphocytes (see page 13, lines 9-10, in particular), (3) performing first-strand cDNA synthesis (i.e., reverse-transcribing) and DNA encoding antigen-binding fragments (i.e., cDNA) were

amplified by PCR (see page 13, lines 11-14, in particular), (4) cloning the amplified antigen-binding fragments into a vector (see pages 14, lines 26-28, in particular), and (5) recovering the obtained clones (see pages 14-15 and Examples 2-3, in particular) (see also pages 10-12 for above steps), which is the identical process of present claim 25 for obtaining the conventional VH camelid domains. Thus, it appears that Frenken et al [b] have produced a cDNA library that necessarily contains antigen-binding fragments that are identical to those recited in the present claims. Since the Patent and Trademark Office does not have the facilities for examining and comparing the claimed cDNA library of with the cDNA library of Frenken et al [b], the burden of proof is upon the Applicants to show a distinction between the structural and functional characteristics of the claimed cDNA library and the cDNA library of the prior art, both produced from identical starting material (i.e., lymphocytes from a non-immunized llama) and produced by an identical process, i.e., isolating lymphocytes from a non-immunized llama, isolating total RNA from the lymphocytes, reverse transcribing the RNA and amplifying the cDNA sequences coding for the antigen-binding fragments (i.e., RT-PCR), cloning the amplified cDNA into a vector and recovering the obtained clones. See In re Best, 562 F.2d 1252, 195 U.S.P.Q. 430 (CCPA 197) and Ex parte Gray, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.).

9. The rejection of claims 25-30 under 35 U.S.C. 103(a) as being unpatentable over Casterman et al (WO 94/04678, 3/3/1994) in view of McCafferty et al (U.S. Patent

6,172,197 B1, filed 6/7/1995) and Krebber et al (FEBS Letters, 377:227-231, 1995) is maintained.

The response filed 10/3/05 provides a technical discussion of the differences between conventional variable heavy domains (VH) and VHH fragments. Applicant points out that VHH are structurally distinct from conventional VHs, which normally exist as part of the conventional four-chain immunoglobulin. Applicant submits that conventional heavy chain domains (VHs) are different from VHHs. This has been fully considered but is not found persuasive. First, the claimed camelid cDNA library recites that it comprises antigen-binding fragments of conventional variable heavy domains of camelid antibodies, which is inclusive to conventional VH and VHH in the library. Applicant is reminded that the transitional term "comprising" is inclusive or open-ended and does not exclude additional, unrecited elements or method steps (see MPEP 2111.03). Additionally, the dependent claims still recite that each antigen-binding fragment of the cDNA library comprises the "variable heavy domain (VHH or VH)" of the antibody, which clearly encompasses both conventional VHs and VHHs in the cDNA library. Further, Casterman et al teach a cDNA library encoding a VHH obtained by (1) isolating lymphocytes from a biological sample from a Camelid (i.e., lama) without previous immunization (see page 24, in particular), (2) isolating poly A RNA from the lymphoid cells; it is inherent that poly A RNA isolation is subsequent to the isolation of total RNA, (3) synthesizing cDNA using reverse-transcriptase, (4) amplifying the cDNA, (5) cloning the amplified sequence into a vector, and (6) recovering the clones (see page 21 and claim 38, in particular), which is the identical process of present claim 25

for obtaining the conventional VH camelid domains. Thus, it appears that Casterman et al have produced a cDNA library that necessarily contains antigen-binding fragments that are identical to those recited in the present claims. Since the Patent and Trademark Office does not have the facilities for examining and comparing the claimed cDNA library of with the cDNA library of Casterman et al, the burden of proof is upon the Applicants to show an unobvious distinction between the structural and functional characteristics of the claimed cDNA library and the cDNA library of the prior art, both produced from identical starting material (i.e., lymphocytes from a non-immunized llama) and produced by an identical process, i.e., isolating lymphocytes from a non-immunized llama, isolating total RNA from the lymphocytes, reverse transcribing the RNA and amplifying the cDNA sequences coding for the antigen-binding fragments (i.e., RT-PCR), cloning the amplified cDNA into a vector and recovering the obtained clones. See In re Best, 562 F.2d 1252, 195 U.S.P.Q. 430 (CCPA 197) and Ex parte Gray, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.).

Applicant does not challenge the combination of the references cited. Therefore, the rejection is maintained for reasons already of record.

10. The rejection of claims 25-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Frenken et al [a] (US Patent 6,399,763 B1) in view of McCafferty et al (U.S. Patent 6,172,197 B1, filed 6/7/1995) and Krebber et al (FEBS Letters, 377:227-231, 1995) is maintained.

Applicant argues as above for Frenken et al [a] and the Examiner's arguments above for Frenken et al [a] apply here as well. Further, Applicant does not challenge

the combination of the references cited. Therefore, the rejection is maintained for reasons already of record.

11. The rejection of claims 25-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Frenken et al [b] (WO 99/37681, 7/29/1999) in view of McCafferty et al (U.S. Patent 6,172,197 B1, filed 6/7/1995) and Krebber et al (FEBS Letters, 377:227-231, 1995) is maintained.

Applicant argues as above for Frenken et al [b] and the Examiner's arguments above for Frenken et al [b] apply here as well. Further, Applicant does not challenge the combination of the references cited. Therefore, the rejection is maintained for reasons already of record.

12. The rejection of claims 25-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hoogenboom et al (Immunotechnology 4:1-20, 1998) in view of Lauwereys et al (The EMBO Journal, 17(13):3512-3520, 1998) and Krebber et al (FEBS Letters, 377:227-231, 1995) is maintained.

The response filed 10/3/05 provides a technical discussion of the differences between conventional variable heavy domains (VH) and VHH fragments. Applicant points out that VHH are structurally distinct from conventional VHs, which normally exist as part of the conventional four-chain immunoglobulin. Applicant submits that conventional heavy chain domains (VHs) are different from VHHs as described by the cited art. This has been fully considered but is not found persuasive. First, the claimed

camelid cDNA library recites that it comprises antigen-binding fragments of conventional variable heavy domains of camelid antibodies, which is inclusive to conventional VH and VHH in the library. Applicant is reminded that the transitional term "comprising" is inclusive or open-ended and does not exclude additional, unrecited elements or method steps (see MPEP 2111.03). Additionally, the dependent claims still recite that each antigen-binding fragment of the cDNA library comprises the "variable heavy domain (VHH or VH)" of the antibody, which clearly encompasses both conventional VHs and VHHs in the cDNA library. Further, even if the claims were amended to exclude VHHs, the combined teachings of Hoogenboom et al and Lauwereys et al and Krebber et al as set forth in the previous Office Action would have motivated one of ordinary skill in the art at the time the invention was made to produce a cDNA library encoding antibodies from a non-immunized camelid source comprising the steps of isolating lymphocytes, isolating RNA for the lymphocytes, synthesizing cDNA and amplifying the cDNA by PCR, cloning the amplified cDNA into a vector and recovering the obtained clones, which is the identical process of present claim 25 for obtaining the conventional VH camelid domains. Thus, it appears that Hoogenboom et al and Lauwereys et al and Krebber et al have produced a cDNA library that necessarily contains antigen-binding fragments that are identical to those recited in the present claims. Since the Patent and Trademark Office does not have the facilities for examining and comparing the claimed cDNA library of with the cDNA library of Hoogenboom et al and Lauwereys et al and Krebber et al, the burden of proof is upon the Applicants to show an unobvious distinction between the structural and functional characteristics of the claimed cDNA

library and the cDNA library of the prior art, both produced from identical starting material (i.e., lymphocytes from a non-immunized llama) and produced by an identical process, i.e., isolating lymphocytes from a non-immunized llama, isolating total RNA from the lymphocytes, reverse transcribing the RNA and amplifying the cDNA sequences coding for the antigen-binding fragments (i.e., RT-PCR), cloning the amplified cDNA into a vector and recovering the obtained clones. See In re Best, 562 F.2d 1252, 195 U.S.P.Q. 430 (CCPA 197) and Ex parte Gray, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.).

Conclusion

13. No claim is allowed.

14. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at (571) 272-0832. The official fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,
David J. Blanchard
571-272-0827

SHEELA HUFF
PRIMARY EXAMINER